

ABSTRACT OF THE DISCLOSURE

A method for targeting a therapeutic agent to a target site in a patient is provided. The method comprises (a) administering to the patient an effective amount for targeting of at least one multispecific targeting protein comprising at least one first binding site which specifically binds to a substance produced by or associated with the target site and present at the target site and at least one second binding site which specifically binds to an epitope on an enzyme, wherein binding between the targeting protein and the enzyme does not interfere with enzyme activity; (b) administering to the patient an effective amount for enzyme activity of the enzyme, such that the targeting protein binds the enzyme to form a targeting protein-enzyme conjugate *in situ*; (c) administering to the patient at least one serum-soluble prodrug composition, wherein the enzyme administered in step (b) acts on the prodrug to release a therapeutic agent that is less soluble in serum than the prodrug, and wherein the therapeutic agent partitions out at the target site such that it accretes at the target site to a greater extent than would the prodrug, thereby providing therapeutic agent at the target site. One or more optional clearing agents may be administered before or after the enzyme. In an alternative embodiment, the targeting protein-enzyme conjugate is made *in vitro* and administered in a single step. Injectable preparations and kits for carrying out the methods also are provided.

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